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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,678	HU ET AL.	
	Examiner	Art Unit	
	KADE ARIANI	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on January 25, 2008, has been received and entered.

Claims 1-47 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Applicant's arguments, filed on 1/25/2008, with respect to the rejection of claims 1, 15, 29, and 41 under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. Therefore, the rejection is withdrawn.

Claims 11-13 recite the limitation "wherein the mono-disperse nanoparticles..." and claim 29 recites the limitation "...the mono-dispersed IPN..." there is insufficient antecedent basis for the cited limitations in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102() that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-10 under 35 U.S.C. 102(b) as being anticipated by Kubota et al. (Journal of Applied Polymer Science, 1998, Vol. 70, p.1027-1034), is withdraw due to applicant's amendments to the claims filed on 1/25/2008.

Claims 1, 4-10, and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Dhara et al. (Macromol Chem. Phys. 2001, Vol. 202, p.3617-3623).

Claims 1, 4-10, and 13-14 are drawn an aqueous dispersion of hydrogel nanoparticles comprising, interpenetrating polymer network (IPN) nanoparticles wherein each IPN nanoparticles comprises a first polymer network interpenetrating a second polymer network; and an aqueous medium, the hydrogel can undergo a reversible gelation in response to a change in stimulus applied thereon, the stimulus is a change in temperature, Tg is about 34ºC, the first polymer comprises poly (-N-isopropylacrylamide) and the second polymer comprises poly (acrylic acid), weight ratio of about 1:1.88, and total polymer concentration from about 1.25 wt% to about 5.25 wt% in distilled water.

Dhara et al. disclose an aqueous dispersion of hydrogel nanoparticles comprising, interpenetrating polymer network (IPN) nanoparticles wherein each IPN nanoparticles comprises a first polymer network interpenetrating a second polymer network; and an aqueous medium, the first polymer comprises poly (-N-isopropylacrylamide) and the second polymer comprises poly (acrylic acid), total polymer concentration 2 wt %, weight ratio 2:1 (p.3618 1st column 2nd an d 3rd paragraphs), the hydrogel can undergo a reversible gelation in response to a change in

stimulus applied thereon, the stimulus is a change in temperature, Tg is about 34°C (p. 3618 2nd column , 2nd and 3rd paragraphs).

Dhara et la. therefore clearly anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1- 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dhara et al. (Macromol Chem. Phys. 2001, Vol. 202, p.3617-3623) in view of Gan & Lyon (J. Am. Chem. Soc., 2001, Vol. 123, No. 31, p.7511-7517) and Hennink & Nostrum (Advanced Drug Delivery, 2002, Vol. 13, p.13-36) and further in view of Kubota et al. (Journal of Applied Polymer Science, 2001, Vol. 80, p.789-805).

Claims 1-14, and 41-47 are drawn to an aqueous dispersion of hydrogel nanoparticles comprising, interpenetrating polymer network (IPN) nanoparticles wherein each IPN nanoparticles comprises a first polymer network interpenetrating a second polymer network; and an aqueous medium, a biologically active material, a drug, Tg is about 34°C, the first polymer comprises poly (-N-isopropylacrylamide) and the second polymer comprises poly (acrylic acid), a uniformed sized hydrodynamic radius in the

range of 75 nm to about 200 nm, weight ratio of about 1:1.88, total polymer concentration from about 1.25 wt% to about 5.25 wt% in distilled water, a nanocluster of cross-linked IPN nanoparticles comprising: at least two IPN nanoparticles linked by a cross-linking group, a first polymer network interpenetrating a second polymer network, the cross linking group is adipic acid dihydrazide, wherein each IPN nanoparticles have a uniformed sized and an have an average hydrodynamic radius in the range of 155 nm to about 1000 nm.

Claims 15-40 are drawn to a method of preparing an IPN comprising, providing a first polymer nanoparticles prepared by mixing first monomer, a surfactant, a first cross linking agent, and first initiator at a first temperature, adding to the first mono-dispersed polymer nanoparticles a second monomer, a second cross linking agent, a second initiator and an activator, mixing the nanoparticles solution for a period of time at a second temperature, isolating the IPN nanoparticles, mixing the isolated IPN with a biologically active material at a third temperature, N, N'-methylenebisacrylamide (cross linking agent), potassium persulfate (1^{st} initiator) at 70°C (1^{st} temperature), poly (acrylic acid) (2^{nd} monomer), ammonium persulfate (2^{nd} initiator), and TEMED (activator), mixing for about 120 minutes at about 21°C (2^{nd} temperature), isolating the IPN, mixing the isolated IPN with a biologically active material at a third temperature at about 33°C, a method of preparing a nanocluster of cross-linked IPN nanoparticles, comprising; providing a dispersion of IPN nanoparticles, adding a first cross linking agent and a second cross linking agent to the dispersion of the IPN nanoparticles, heating the IPN cross linking solution to a first temperature for a period of time, wherein the IPN nanoparticles have uniformed size and comprise a first polymer network

interpenetrating a second polymer network, mixing the nanocluster of cross-linked IPNs with a biologically active material at a second temperature, the first polymer comprises of poly(-N-isopropylacrylamide) and the second polymer comprises poly(acrylic acid), first cross-linking agent comprises EDAC and second cross linking agent comprises adipic acid dihydrazide, heating at a first temperature, about 44°C, for about 25-45 min (33-37 min), mixing cross-linked IPNs with a biologically active material at about 33°C, and hydrodynamic radius in the range from 225 nm to about 240 nm.

Dhara et al. teach an aqueous dispersion of hydrogel nanoparticles comprising, interpenetrating polymer network (IPN) nanoparticles wherein each IPN nanoparticles comprises a first polymer network interpenetrating a second polymer network; and an aqueous medium, the first polymer comprises poly (-N-isopropylacrylamide) and the second polymer comprises poly (acrylic acid), total polymer concentration 2 wt %, weight ratio 2:1 (p.3618 1st column 2nd an d 3rd paragraphs), the hydrogel can undergo a reversible gelation in response to a change in stimulus applied thereon, the stimulus is a change in temperature, Tg is about 34°C (p. 3618 2nd column , 2nd and 3rd paragraphs).

Dhara et al. teach a method of preparing an IPN comprising, providing a first mono-dispersed polymer nanoparticles prepared by mixing first monomer, a first cross linking agent, and first initiator at a first temperature, adding to the first mono-dispersed polymer nanoparticles a second monomer, a second cross linking agent, a second initiator and an activator, mixing the nanoparticles solution for a period of time at a second temperature, isolating the IPN nanoparticles, , N, N'-methylenebisacrylamide (BIS), and potassium persulfate, poly (acrylic acid), ammonium persulfate, and TEMED,

at about 21°C (ambient temperature) (p.3618, 1st column 2nd & 3rd paragraphs, and 5th paragraph).

Dhara et al. do not teach the hydrogel nanoparticles further comprising a drug, mixing with a surfactant, mixing the isolated IPN with a biologically active material at a third temperature, and is silent about the size and hydrodynamic radius. However, Gan & Lyon teach application of hydrogel nanoparticles for drug delivery, and polymerization by mixing with SDS (surfactant). Gan & Lyon further teach the size of the particles was controlled via varying concentration of SDS during polymerization (p.7512, 2nd column line 9, and last paragraph lines 5-7).

Dhara et al. do not teach cross-linking agents EDAC and adipic acid dihydrazide. However, at the time the invention made, EDAC, a highly efficient reagent to crosslink water-soluble polymers with amide bonds, and adipic acid dihydrazide, a less toxic cross linking agent for aldehyde-mediated crosslinking of polymers), were both being used in the art as crosslinking agents for hydrogel preparation (Hennink & Nostrum, p. 19 column 1& Fig 4., p.20, column 1).

Furthermore, Dhara et al. teach the incorporation of acrylic acid network imparts anionic character to the IPNs. PNIPA is a temperature sensitive polymer whereas PAA is pH sensitive. The presence of poly (acrylic acid) (PAA) network makes the system highly swelling hydrogel. The effect of PNIPA and its shrinkage above transition temperature is only observed in compositions with high PNIPA content. As PAA content increases the IPN remains uniformly swollen at all temperatures (p.3618 2nd column 2nd paragraph).

Further motivation is in Kubota et al. who teach the application of stimuli and swelling-controlled hydrogels in drug delivery and the need for gels that can change the release rate of incorporated drugs according to the stimuli.

Therefore, a person of ordinary skill in the art would have been motivated to modify the method and the hydrogel nanoparticles as taught by Dhara et al. according to the teachings of Gan & Lyon and Hennink & Nostrum to provide an aqueous dispersion of hydrogel nanoparticles and a method of preparing hydrogel nanoparticles. The motivation as taught by Kubota et al. would be to provide stimuli and swelling-controlled hydrogels that can change the release rate of incorporated drugs according to the stimuli.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

Kade Ariani
Examiner
Art Unit 1651